

(FILE 'HOME' ENTERED AT 14:22:06 ON 10 DEC 2002)

FILE 'BIOSIS, CAPLUS, SCISEARCH, LIFESCI, EMBASE' ENTERED AT 14:23:40 ON
10 DEC 2002

L1 4160 S BROMELAIN
L2 691 S L1 AND BLOOD
L3 436 DUPLICATE REMOVE L2 (255 DUPLICATES REMOVED)
L4 36 S L2 (A) COAGULATION
L5 27 DUPLICATE REMOVE L4 (9 DUPLICATES REMOVED)

=>

also: USPATFVLL, PATOSWO, EUROPATFVLL & JAP10

IEN USE OF BROMELAIN PROTEASES FOR INHIBITING BLOOD COAGULATION.
 TIDE VERWENDUNG VON BROMELAINPROTEASEN ZUR HEMMUNG DER BLUTGERINNUNG.
 TIFR UTILISATION DE BROMELAINE PROTEASES POUR EMPECHER LA COAGULATION DU SANG.
 IN MAURER, Rainer, Schopenhauerstrasse 93, D-14129 Berlin, DE;
 ECKERT, Klaus, Karower Chaussee 215, D-13125 Berlin, DE;
 GRABOWSKA, Edyta, Aristotelessteig 6, D-10318 Berlin, DE;
 ESCHMANN, Klaus, Lothringerstrasse 26, D-66271 Kleinblittersdorf, DE
 PA URSAPHARM Arzneimittel GmbH & Co. KG, Industriestrasse, D-66129 Saarbruecken, DE
 PAN 1383191
 AG Becker Kurig Straus, Patentanwaelte Bavariastrasse 7, 80336 Muenchen, DE
 AGN 101571
 OS BEPB2002058 EP 1096951 B1 0011
 SO Wila-EPS-2002-H33-T1
 DT Patent
 LA Anmeldung in Deutsch; Veroeffentlichung in Deutsch
 DS R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE
 PIT EPB1 EUROPAEISCHE PATENTSCHRIFT (Internationale Anmeldung)
 PI EP 1096951 B1 20020814
 OD 20010509
 AI EP 1998-942559 19980715
 RLI WO 98-EP4406 980715 INTAKZ
 WO 0003729 000127 INTPNR
 REP WO 98-38291 A
 REN TAUSSIG S J ET AL: "Bromelain, the enzyme complex of pineapple (ananas comosus) and its clinical application. An update" JOURNAL OF ETHNOPHARMACOLOGY, Bd. 22, Nr. 2, 1988, Seite 191-203 XP002097864
 HARRACH T ET AL: "ISOLATION AND PARTIAL CHARACTERIZATION OF BASIC PROTEINASES FROM STEM BROMELAIN" JOURNAL OF PROTEIN CHEMISTRY, Bd. 14, Nr. 1, Januar 1995, Seiten 41-52, XP002069063 in der Anmeldung erwaeht
 SUNNY M C ET AL: "Effect of fabrication, sterilization and mediators-blood compatibility of polyurethanes" JOURNAL OF BIOMATERIALS APPLICATIONS, Bd. 6, Nr. 3, Januar 1992, Seite 261-273 XP002097865
 DATABASE WPI Derwent Publications Ltd., London, GB; AN 89-019644
 XP002097957 & JP63295515 A (KAO CORP), Januar 1988
 L6 ANSWER 11 OF 45 USPATFULL
 AN 2001:218007 USPATFULL
 TI Lipase-containing composition and methods of use thereof
 IN Margolin, Alex, Newton, MA, United States
 Shenoy, Bhami, Woburn, MA, United States
 PI US 2001046493 A1 20011129
 AI US 2001-791947 A1 20010222 (9)
 PRAI US 2000-184517P 20000224 (60)
 DT Utility
 FS APPLICATION
 LREP Ivor R. Elrifi, Ph.D., MINTZ, LEVIN, COHN, FERRIS,, GLOVSKY and POPEO, P.C., One Financial Center, Boston, MA, 02111
 CLMN Number of Claims: 47
 ECL Exemplary Claim: 1
 DRWN 2 Drawing Page(s)
 LN.CNT 914
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

6 ANSWER 28 OF 45 USPATFULL
AN 1998:68989 USPATFULL
TI Medical application of bromelain
IN Barnwell, Stephen George, Chester, England
PA Cortecs Limited, Great Britain (non-U.S. corporation)
PI US 5767066 19980616
WO 9522348 19950824
AI US 1996-696918 19960819 (8)
WO 1995-GB352 19950221
19960819 PCT 371 date
19960819 PCT 102(e) date
PRAI GB 1994-3344 19940222
DT Utility
FS Granted
EXNAM Primary Examiner: Jordan, Kimberly
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 598
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 37 OF 45 PATOSWO COPYRIGHT 2002 WILA

AN 1995:68409 PATOSWO ED 19950129 EW 199501 FS OS

TI MEDICAL USE OF STEM **BROMELAIN** PROTEASE.

IN MYNOTT, TRACEY, LEHANNE, GB

PA CORTECS LIMITED, GB

SO PCT-GAZETTE-950105

DT Patent

LA Application in English

DS W @@; W AT; W AU; W BB; W BG; W BR; W BY; W CA; W CH; W CN; W CZ; W DE;
W DK; W ES; W FI; W GB; W GE; W HU; W JP; W @@; W KG; W KP; W KR; W KZ;
W LK; W LU; W LV; W MD; W MG; W MN; W MW; W NL; W NO; W NZ; W PL; W PT;
W RO; W RU; W SD; W SE;
RW AT; RW BE; RW CH; RW DE; RW DK; RW ES; RW FR; RW GB; RW GR; RW IE;

RW IT; RW LU; RW MC; RW NL; RW PT; RW SE; RW BF; RW BJ; RW CF; RW CG; RW
CI; RW CM; RW GA; RW GN; RW ML; RW MR; RW NE; RW SN; RW TD; RW TG

PIT WOA1 PCT-PUBLICATION

PI WO 9500169 A1 19950105

OD 19950105

AI WO 1994-GB1368 19940624

PRAI GB 1993-13188 19930625

in IDS

S ANSWER 24 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 1979:483367 CAPLUS
DN 91:83367
TI **Bromelain**, a thiolprotease from pineapple stem, depletes high
molecular weight kininogen by activation of Hageman factor (factor XII)
AU Ohishi, Sachiko; Uchida, Yasuhiro; Ueno, Akinori; Katori, Makoto
CS Sch. Med., Kitasato Univ., Sagamihara, 228, Japan
SO Thrombosis Research (1979), 14(4-5), 665-72
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English

5 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 1983:2358 CAPLUS
DN 98:2358
TI Fluid phase activation of Hageman factor (factor XII) in citrated human
plasma by **bromelain**: an application to the indirect enzymic
assay for Hageman factor
AU Ohishi, Sachiko
CS Sch. Pharm. Sci., Kitasato Univ., Tokyo, Japan
SO Thrombosis Research (1982), 27(5), 619-23
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English

L6 ANSWER 7 OF 45 USPATFULL
AN 2002:1315 USPATFULL
TI Component of stem bromelain
IN Mynott, Tracey Lehanne, Richmond, UNITED KINGDOM
Engwerda, Christian, Richmond, UNITED KINGDOM
Peek, Keith, Ewloe, UNITED KINGDOM
PA Provalis UK Limited, Flintshire, UNITED KINGDOM (non-U.S. corporation)
PI US 6335427 B1 20020101
AI US 1999-382689 19990825 (9)
RLI Continuation of Ser. No. WO 1998-GB592, filed on 25 Feb 1998
PRAI GB 1997-3827 19970225
GB 1997-3850 19970225
GB 1997-4252 19970228
DT Utility
FS GRANTED
EXNAM Primary Examiner: Stucker, Jeffrey
LREP Sterne, Kessler, Goldstein & Fox, P.L.L.C.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 18 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 1450

S ANSWER 1 OF 27 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
 AN 2002137515 EMBASE
 TI A follow-up survey of the use of complementary and alternative medicines
 by surgical patients.
 AU Norred C.L.
 CS C.L. Norred, Department of Anesthesiology, Univ. of Colorado Hlth. Sci.
 Ctr., Denver, CO, United States
 SO Journal of the American Association of Nurse Anesthetists, (2002) 70/2
 (119-125).
 Refs: 27
 ISSN: 0094-6354 CODEN: JANAAU
 CY United States
 DT Journal; Article
 FS 017 Public Health, Social Medicine and Epidemiology
 024 Anesthesiology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LA English
 SL English
 AB This study investigated the use of complementary and alternative
 medicines
 by surgical patients at the University of Colorado Health Sciences
 Center,
 Denver. Elective surgical outpatients were randomly surveyed with
 anonymous self-report questionnaires during day-surgery admission about
 alternative medicines taken during the 2 weeks before surgery; 496 of 500
 questionnaires were completed and returned. Of the patients, 37% reported
 62 types of herbs, 59% reported 14 types of vitamins, 45% reported 36
 types of dietary supplements, and 1% reported taking 5 types of
 homeopathics. A total of 73.4% of patients took alternative medicines
 preoperatively (range, 1-44 medicines). After a literature review, the
 alternative medicines were categorized for potential interactions with
 anesthetic drugs. Alternative medicines that have inhibitory effects on
 the **coagulation** cascade were reported by 40% of surgical
 patients. The following percentages of patients took medicines that
 affect
blood pressure, 32%; affect cardiac function, 20%; cause sedation,
 17%; or have potential to alter electrolyte levels, 9%. Herbs recognized
 to interact with pharmaceuticals were consumed by 23% of patients.
 Further
 research, education, and improved communication are needed to safely
 integrate alternative medicines for surgical patients.
 CT Medical Descriptors:
 *alternative medicine
 *surgical patient
 questionnaire
 herb
 follow up
 diet supplementation
 homeopathy
blood clotting
 anesthesia
 garlic
 Echinacea
 cranberry
 Arnica montana
 Calendula
 Glycyrrhiza
 Hypericum perforatum
 Aloe

ginseng
 Ginkgo biloba
 celery
 bleeding: SI, side effect
 human
 male
 female
 major clinical study
 clinical trial
 randomized controlled trial
 controlled study
 article
 Drug Descriptors:
 vitamin: AE, adverse drug reaction
 anesthetic agent
 electrolyte: EC, endogenous compound
 calcium
 glucosamine
 sulfur
 phosphorus
 Aconitum extract
 thrombocyte activating factor: EC, endogenous compound
 prostaglandin synthase: EC, endogenous compound
 arachidonic acid: EC, endogenous compound
 fibrinogen: EC, endogenous compound
 plasminogen: EC, endogenous compound
 adenosine diphosphate: EC, endogenous compound
 prostaglandin E2: EC, endogenous compound
 thromboxane A2: EC, endogenous compound
 prostacyclin: EC, endogenous compound
 ubidecarenone
 kava: IT, drug interaction
 valerian: IT, drug interaction
 melatonin
 4 aminobutyric acid receptor: EC, endogenous compound
 bromelain: IT, drug interaction
 fish oil
 primrose oil
 ephedrine: IT, drug interaction
 lavender oil
 sertraline: AE, adverse drug reaction
 herbaceous agent: AE, adverse drug reaction
 unindexed drug

RN (calcium) 7440-70-2; (glucosamine) 3416-24-8, 4607-22-1; (sulfur)
 13981-57-2, 7704-34-9; (phosphorus) 7723-14-0; (thrombocyte activating
 factor) 64176-80-3, 65154-06-5; (prostaglandin synthase) 39391-18-9,
 59763-19-8, 9055-65-6; (arachidonic acid) 506-32-1, 6610-25-9, 7771-44-0;
 (fibrinogen) 9001-32-5; (plasminogen) 9001-91-6; (adenosine diphosphate)
 20398-34-9, 58-64-0; (prostaglandin E2) 363-24-6; (thromboxane A2)
 57576-52-0; (prostacyclin) 35121-78-9, 61849-14-7; (ubidecarenone)
 303-98-0; (valerian) 8057-49-6; (melatonin) 73-31-4; (bromelain)
 37189-34-7, 9001-00-7; (fish oil) 8016-13-5; (primrose oil) 65546-85-2;
 (ephedrine) 299-42-3, 50-98-6; (lavender oil) 8000-28-0, 8022-15-9;
 (sertraline) 79617-96-2
 CN Zolof

=>

L5 ANSWER 12 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
INC.DUPLICATE

3

AN 1997:519010 BIOSIS

DN PREV199799818213

TI Influence of the therapeutically used enzymes **bromelain**, papain
and trypsin on the **blood coagulation** in vitro.

AU Alban, S. (1); Franz, M. E.; Franz, G.

CS (1) Inst. Pharmacy, Univ. Regensburg, D-93040 Regensburg Germany

SO Pharmaceutical and Pharmacological Letters, (1997) Vol. 7, No. 2-3, pp.
59-62.

ISSN: 0939-9488.

DT Article

LA English

L5 ANSWER 15 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
INC.DUPLICATE

5

AN 1988:268606 BIOSIS

DN BA86:7850

TI **BROMELAIN** THE ENZYME COMPLEX OF PINEAPPLE ANANAS-COMOSUS AND ITS
CLINICAL APPLICATION AN UPDATE.

AU TAUSSIG S J; BATKIN S

CS CANCER RES. CENT. HAWAII, UNIV. HAWAII, 1236 LAUHALA ST., 503, HONOLULU,
HAWAII.

SO J ETHNOPHARMACOL, (1988) 22 (2), 191-204.

CODEN: JOETD7. ISSN: 0378-8741.

FS BA; OLD

LA English

AB After a short description of the uses of pineapple as folk medicine by
the

natives of the tropics, the more important new pharmaceutical
applications

of **bromelain**, reported between 1975 and 1978 are presented.

Although the exact chemical structure of all active components of
bromelain is not fully determined, this substance has shown
distinct pharmacological promise. Its properties include: interference
with growth of malignant cells; inhibition of platelet aggregation;
fibrinolytic activity; antiinflammatory action; skin debridement
properties. These biological functions of **bromelain**, a non-toxic
compound have therapeutic values in modulating: tumor growth;
blood coagulation; inflammatory changes; debridement of
third degree burns; enhancement of absorption of drugs. The mechanism of
action of **bromelain** affecting these varied biological effects
relates in part to its modulation of the arachidonate cascade.

CC Biochemical Studies - Lipids 10066

Pathology, General and Miscellaneous - Inflammation and Inflammatory
Disease 12508

Metabolism - Lipids *13006

Blood, Blood-Forming Organs and Body Fluids - General; Methods 15001

Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods
18001

Integumentary System - General; Methods 18501

Pharmacology - General *22002

Pharmacology - Blood and Hematopoietic Agents *22008

Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs

*22012

Pharmacology - Integumentary System, Dental and Oral Biology *22020

Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008

Plant Physiology, Biochemistry and Biophysics - Enzymes 51518

Plant Physiology, Biochemistry and Biophysics - Chemical Constituents
*51522

Pharmacognosy and Pharmaceutical Botany *54000

BC Muridae 86375

IT Miscellaneous Descriptors

MOUSE ARACHIDONATE HEMATOLOGIC-DRUG ANTINEOPLASTIC-DRUG

ANTIINFLAMMATORY-DRUG DERMATOLOGICAL-DRUG

RN 506-32-1 (ARACHIDONATE)

9001-00-7Q, 37189-34-7Q (**BROMELAIN**)

5 ANSWER 12 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
3

AN 1997:519010 BIOSIS

DN PREV199799818213

TI Influence of the therapeutically used enzymes **bromelain**, papain
and trypsin on the **blood coagulation** in vitro.

AU Alban, S. (1); Franz, M. E.; Franz, G.

CS (1) Inst. Pharmacy, Univ. Regensburg, D-93040 Regensburg Germany

SO Pharmaceutical and Pharmacological Letters, (1997) Vol. 7, No. 2-3, pp.
59-62.

ISSN: 0939-9488.

DT Article

LA English

AB The therapeutically used enzymes **bromelain**, papain, and trypsin
are shown to be bioavailable and to exhibit proteolytic activity after
oral administration. In order to answer the question if such enzymes
interact with endogenous enzymatic processes, their influence on the
blood coagulation was examined in vitro as a basis for
the corresponding in vivo study. For this purpose, the **coagulation**
time of supplemented plasma was determined in the global
coagulation assays. i.e. activated partial thromboplastin time
(APTT), prothrombin time, Heptest, and thrombin time. According to their
specific nature, the three proteolytic enzymes interact with the
blood coagulation in a different manner in vitro.
However, the effective concentrations are very high and usually not found
in vivo after oral administration of these enzymes.

CC Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Enzymes - Physiological Studies *10808

Blood, Blood-Forming Organs and Body Fluids - General; Methods 15001

Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies
*15002

Pharmacognosy and Pharmaceutical Botany *54000

BC Hominidae *86215

IT Major Concepts

Biochemistry and Molecular Biophysics; **Blood** and Lymphatics
(Transport and Circulation); Enzymology (Biochemistry and Molecular
Biophysics); Pharmacognosy (Pharmacology)

IT Chemicals & Biochemicals

BROMELAIN; PAPAINE; TRYPSIN; PROTHROMBIN; THROMBIN

IT Miscellaneous Descriptors

ACTIVATED PARTIAL THROMBOPLASTIN TIME; **BLOOD** AND LYMPHATICS;

BLOOD COAGULATION; **BROMELAIN**; DIAGNOSTIC

METHOD; PAPAINE; PHARMACOGNOSY; PROTHROMBIN TIME; THROMBIN TIME;

TRYPSIN

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Superterms

animals; chordates; humans; mammals; primates; vertebrates

RN 9001-00-7Q (**BROMELAIN**)

37189-34-7Q (**BROMELAIN**)

150977-36-9Q (**BROMELAIN**)

9001-73-4 (PAPAINE)

9002-07-7 (TRYPSIN)

9001-26-7 (PROTHROMBIN)

9002-04-4 (THROMBIN)

=>

5 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2002 ACS

AN 2000:68352 CAPLUS

DN 132:117543

TI Use of **bromelain** proteases for inhibiting **blood coagulation**

IN Maurer, Rainer; Eckert, Klaus; Grabowska, Edyta; Eschmann, Klaus

PA Ursapharm Arzneimittel G.m.b.H., Germany

SO PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DT Patent

LA German

IC ICM A61K038-48

CC 1-8 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000003729	A1	20000127	WO 1998-EP4406	19980715
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2333252	AA	20000127	CA 1998-2333252	19980715
	AU 9890661	A1	20000207	AU 1998-90661	19980715
	EP 1096951	A1	20010509	EP 1998-942559	19980715
	EP 1096951	B1	20020814		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	AT 222121	E	20020815	AT 1998-942559	19980715
PRAI	WO 1998-EP4406	A	19980715		
AB	Bromelain proteases are used for inhibiting the blood coagulation system, notably for stimulating plasmin prodn., inhibiting fibrin prodn. and inhibiting the adhesion of human thrombocytes to endothelial cells. The basic proteases, which can be isolated from pure bromelain , have proved to be esp. suitable proteases.				
ST	bromelain protease blood coagulation inhibition				
IT	Platelet (blood) (adhesion; bromelain proteases for inhibiting blood coagulation)				
IT	Anticoagulants Fibrinolytics (bromelain proteases for inhibiting blood coagulation)				
IT	Fibrins RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (bromelain proteases for inhibiting blood coagulation)				
IT	Blood vessel (endothelium, platelet adhesion; bromelain proteases for inhibiting blood coagulation)				
IT	Cell adhesion (platelet; bromelain proteases for inhibiting blood coagulation)				
IT	158701-41-8	256229-06-8			

L5 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2002 ACS

AB **Bromelain** proteases are used for inhibiting the **blood coagulation** system, notably for stimulating plasmin prodn., inhibiting fibrin prodn. and inhibiting the adhesion of human thrombocytes to endothelial cells. The basic proteases, which can be isolated from pure **bromelain**, have proved to be esp. suitable proteases.

L5 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 1984:483329 CAPLUS
DN 101:83329
TI Effect of **bromelain** as an anticoagulant and its significance as
an antimetastatic
AU Taussig, S. J.
CS Dep. Food Sci. Human Nutr., Univ. Hawaii, Honolulu, HI, USA
SO Erfahrungsheilkunde (1984), 33(6), 342-8
CODEN: ERFAAK; ISSN: 0014-0082
DT Journal; General Review
LA German

Journal of Ethnopharmacology, 22
blood coagulation
inhibition of: platelet aggregation
fibrinolytic activity

L1 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:312148 CAPLUS

DOCUMENT NUMBER: 129:78309

TITLE: Isolation and characterization of two forms of an acidic bromelain stem proteinase

AUTHOR(S): Harrach, Tibor; **Eckert, Klaus**; Maurer, H. Rainer; Machleidt, Irmgard; Machleidt, Werner; Nuck, Rolf

CORPORATE SOURCE: Institut fur Pharmazie, Abteilung Pharmazeutische Biochemie, Freie Universitat Berlin, Berlin, D-12169, Germany

SOURCE: Journal of Protein Chemistry (1998), 17(4), 351-361

CODEN: JPCHD2; ISSN: 0277-8033

PUBLISHER: Plenum Publishing Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two forms of an acidic bromelain isolated from crude bromelain, an ext. from pineapple stem, were found by a 2-step FPLC purifn. procedure. The basic main components were removed by cation-exchange chromatog. and the breakthrough fraction was further resolved by anion-exchange chromatog. into 15 protein fractions, only 2 of which, called SBA/a and SBA/b, were proteolytically active. These components were characterized by electrospray mass spectroscopy (ESMS), isoelec. focusing, N-terminal amino

acid sequence anal., monosaccharide anal., and enzymic parameters. The mol. wts. of SBA/a and SBA/b were detd. by ESMS to be 23,550 and 23,560, resp. The pI values of the 2 bands of SBA/a were 4.8 and 4.9; SBA/b focused as a single band at pI 4.8. Partial N-terminal amino acid sequences (11 residues) were identical to SBA/a and SBA/b and identical with those of stem bromelain, the basic main proteinase of the pineapple stem, and fruit bromelain, the acidic main proteinase of the pineapple fruit. Both components were highly glycosylated; hydrolysis of SBA/a yielded .apprx.2-fold more monosaccharide per protein than SBA/b. The comparison of the catalytic properties of SBA/a with those of SBA/b revealed no relevant differences in the hydrolysis of 3 peptidyl-NH-Mec substrates and in the inhibition profiles using chicken cystatin and

E-64, indicating that these components could be considered as 2 forms of a single enzyme. Both forms were barely inhibited by chicken cystatin and slowly inactivated by E-64, and hence are nontypical cysteine proteinases of the papain superfamily.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

Maurer R

0 -

12/11/02

CAPLUS AUTHOR'S NAME

SEARCH RESULTS

L1 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:290725 CAPLUS

DOCUMENT NUMBER: 131:111159

TITLE: Bromelain proteases reduce human platelet aggregation in vitro, adhesion to bovine endothelial cells and thrombus formation in rat vessels in vivo

AUTHOR(S): Metzsig, Carola; Grabowska, Edyta; Eckert,

Klaus; Rehse, Klaus; Maurer, H. Rainer

CORPORATE SOURCE: Institute of Pharmacy, Free University of Berlin, Berlin, 12169, Germany

SOURCE: In Vivo (1999), 13(1), 7-12

CODEN: IVIVE4; ISSN: 0258-851X

PUBLISHER: International Institute of Anticancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The thiol protease, bromelain, an ext. from pine apple stem, was suggested

to have antithrombotic and anticoagulant activities in vivo. We studied the effects of bromelain on cell size distribution of isolated human platelets in vitro by Coulter Counter measurements. Preincubation of platelets with bromelain (10 .mu.g/mL) completely prevented the thrombin (0.2 U/mL) induced platelet aggregation. Papain was less active in preventing platelet aggregation. In vitro, bromelain (0.1 .mu.g/mL) reduced the adhesion of bound, thrombin stimulated, fluorescent labeled platelets to bovine aorta endothelial cells. In addn., preincubation of platelets with bromelain, prior to thrombin activation, reduced the platelet adhesion to the endothelial cells to the low binding value of unstimulated platelets. On the basis of mass concns., the proteases papain and trypsin were as effective as bromelain. Using a laser thrombosis model, the in vivo effects of orally and i.v. applied

bromelain

on thrombus formation in rat mesenteric vessels were studied. Bromelain, orally applied at 60 mg/kg body wt., inhibited the thrombus formation in

a

time dependent manner, the max. being after 2 h in 11% of arterioles and 6% of venules. I.v. application at 30 mg/kg was slightly more active in reducing thrombus formation in arterioles (13%) and venules (5%), suggesting that orally applied bromelain is biol. active. These results may help to explain some of the clin. effects obsd. after bromelain treatment in patients with thrombosis and related diseases.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT